Claims

1. A substantially pure NES1 polypeptide.

2. The polypeptide of claim 1, comprising an amino acid sequence substantially identical to the sequence shown in Figure 10 (SEQ ID NO: 1).

3. The polypeptide of claim 1, wherein said polypeptide is derived from a mammal.

4. The polypeptide of claim 3, wherein said mammal is a human.

5. Purified DNA comprising a sequence encoding a polypeptide of claim 1.

6. The purified DNA of claim 5, wherein said DNA encodes a human NES1 polypeptide.

6a. The DNA of claim 5, said DNA encoding an amino acid sequence substantially identical to the amino acid sequence shown in Figure 10 (SEQ ID NO: 1).

7. The DNA of claim 5, said DNA comprising a DNA sequence substantially identical to the DNA sequence shown in Figure 11 (SEQ ID NO: 2).

8. A vector comprising the purified DNA of claim 5.

9. A cell comprising the purified DNA of claim 5.

10. A method of producing a recombinant NES1 polypeptide comprising,

providing a cell transformed with DNA encoding a NES1 polypeptide positioned for expression in said cell;

culturing said transformed cell under conditions for expressing said DNA; and

isolating said recombinant NES1 polypeptide.

11. NES1 polypeptide produced by expression of the purified DNA of claim 5.

12. A substantially pure antibody that specifically binds a NES1 polypeptide.

13. A method of diagnosing a mammal for the presence of a malignancy or an increased likelihood of developing a malignancy, said method comprising measuring NES1 gene expression in a sample from said mammal, a decrease in NES1 expression relative to a wild-type sample being an indication that said mammal has a malignancy or has an increased likelihood of developing a malignancy.

14. The method of claim 13, wherein said malignancy is a carcinoma.

15. The method of claim 13, wherein said sample comprises an epithelial cell or a cell of epithelial origin.

16. The method of claim 15, wherein said sample comprises a breast tissue cell.

17. The method of claim 15, wherein said sample comprises a cervical tissue cell.

18. The method of claim 15, wherein said sample comprises a prostate tissue cell.

19. The method of claim 13, wherein said NES1 gene expression is measured by assaying the amount of NES1 polypeptide in said sample.

20. The method of claim 19, wherein said NES1 polypeptide is measured by immunological methods.

21. A kit for diagnosing a mammal for the presence of a malignancy or an increased likelihood of developing a malignancy, said kit comprising a substantially pure antibody that specifically recognizes and binds a NES1 polypeptide.

22. The kit of claim 21, further comprising means for detecting said binding of said antibody to said NES1 polypeptide.

23. The method of claim 13, wherein said NES1 gene expression is measured by assaying the amount of NES1 RNA in said sample.

24. The method of claim 23, wherein said NES1 RNA is measured by hybridization techniques using a NES1-specific nucleic acid sequence.

25. A method of diagnosing a mammal for the presence of a malignancy or an increased likelihood of developing a malignancy, said method comprising isolating a sample of nucleic acid from said mammal and determining whether said nucleic acid comprises a mutated NES1 gene, a

NES1 mutation being an indication that said mammal has a malignancy or has an increased likelihood of developing a malignancy.

26. The method of claim 25, wherein said malignancy is a carcinoma.

27. The method of claim 25, wherein said nucleic acid sample is isolated from an epithelial cell or a cell of epithelial origin.

28. The method of claim 27, wherein said epithelial cell is a breast tissue cell.

29. The method of claim 27, wherein said epithelial cell is a cervical tissue cell.

30. The method of claim 27, wherein said epithelial cell is a prostate tissue cell.

31. A kit for diagnosing a mammal for the presence of a malignancy or an increased likelihood of developing a malignancy, said kit comprising a wild-type NES1 nucleic acid sequence.

32. The kit of claim 31, further comprising means for detecting a mismatch between said wild-type NES1 nucleic acid sequence and a nucleic acid sequence isolated from said mammal to be diagnosed.

33. A method of diagnosing a mammal for the presence of a malignancy or an increased likelihood of developing a malignancy, said method comprising measuring

NES1 protease activity in a sample from said mammal, a decrease in said NES1 protease activity relative to a wild-type sample being an indication that said mammal has a malignancy or has an increased likelihood of developing a malignancy.

34. The method of claim 33, wherein said malignancy is a carcinoma.

35. The method of claim 33, wherein said sample comprises an epithelial cell or a cell of epithelial origin.

36. The method of claim 35, wherein said sample comprises a breast tissue cell.

37. The method of claim 35, wherein said sample comprises a cervical tissue cell.

38. The method of claim 35, wherein said sample comprises a prostate tissue cell.

39. A kit for diagnosing a mammal for the presence of a malignancy or an increased likelihood of developing a malignancy, said kit comprising a substantially pure wild-type NES1 polypeptide.

40. The kit of claim 39, further comprising means for measuring protease activity, whereby the protease activity of said wild-type NES1 polypeptide may be compared to NES1 in a sample from said mammal to be diagnosed.

41. The kit of claim 39, wherein said NES1 polypeptide comprises an amino acid sequence substantially

identical to the amino acid sequence shown in Fig. 10 (SEQ ID NO: 1).

42. A method of treating a mammal with a NES1-associated malignancy, said method comprising administering to said mammal a transgene encoding a NES1 polypeptide.

43. The method of claim 42, wherein said transgene encodes a NES1 polypeptide comprising an amino acid sequence substantially identical to the amino acid sequence shown in Fig. 10 (SEQ ID NO: 1).

44. The method of claim 42, wherein said transgene is administered to said mammal at the site of said malignancy.

45. The method of claim 42, wherein said transgene is included in a viral vector.

46. The method of claim 45, wherein said viral vector is a retrovirus, adenovirus, or adeno-associated virus vector.

47. The method of claim 42, wherein said malignancy is a carcinoma.

48. The method of claim 47, wherein said malignancy is a breast carcinoma.

49. The method of claim 47, wherein said malignancy is a cervical carcinoma.

50. The method of claim 47, wherein said malignancy is a prostate carcinoma.

51. A method of treating a mammal with a NES1-associated malignancy, said method comprising administering to said mammal a NES1 polypeptide in an amount sufficient to inhibit an increase in said malignancy.

52. The method of claim 51, wherein said malignancy is a carcinoma.

53. A therapeutic composition comprising as an active ingredient a NES1 polypeptide according to claim 1, said active ingredient being formulated in a physiologically-acceptable carrier.

54. A method of identifying a modulatory compound which is capable of increasing the expression of a NES1 gene, comprising (a) providing a cell expressing said NES1 gene; and (b) contacting said cell with a candidate compound, an increase in said NES1 expression following contact with said candidate compound identifying a modulatory compound.

55. The method of claim 54, wherein said NES1 gene encodes an amino acid sequence that is substantially identical to the amino acid sequence shown in Fig. 10 (SEQ ID NO: 1).

56. A method of identifying a modulatory compound which is capable of increasing NES1 protease activity, comprising (a) providing a cell expressing said NES1 protease; and (b) contacting said cell with a candidate

compound, an increase in said NES1 protease activity following contact with said candidate compound identifying a modulatory compound.

57. The method of claim 56, wherein said NES1 protease comprises an amino acid sequence substantially identical to the amino acid sequence shown in Fig. 10 (SEQ ID NO: 1).

58. The method of claims 54 or 56, wherein said candidate compound is chosen from a tumor promoter, a differentiation agent, or a cytokine.

59. The method of claim 58, wherein said candidate compound is acts through a protein kinase C signal transduction pathway.

60. The method of claim 59, wherein said candidate compound is chosen from diacylglycerol, retinoic acid, estradiol, di-butyryl cyclic AMP, forskolin, TGFβ, TNF, or IL1.

61. A method of treating a mammal with a disease involving decreased expression of a NES1-encoding gene, said method comprising administering to said patient a modulatory compound that is capable of increasing NES1 expression or protease activity, in an amount sufficient to reduce the symptoms of said disease in said mammal.

62. The method of claim 61, wherein said modulatory compound acts through a protein kinase C signal transduction pathway.

63. The method of claim 62, wherein said modulatory compound is 4,8-phorbol-12-myristate-13-acetate.

64. A NES1 protease.

65. The protease of claim 64, said protease being a serine protease.

66. The protease of claim 64, said protease having an amino acid sequence substantially identical to the sequence shown in Fig. 10 (SEQ ID NO: 1).

67. A method of cleaving a polypeptide comprising contacting said polypeptide with a NES1 polypeptide under conditions sufficient for cleavage.

68. The method of claim 67, said NES1 polypeptide having an amino acid sequence substantially identical to the sequence shown in Fig. 10 (SEQ ID NO: 1).